Date of Approval: March 31, 2012

FREEDOM OF INFORMATION SUMMARY

SUPPLEMENTAL ABBREVIATED NEW ANIMAL DRUG APPLICATION

ANADA 200-455

TYLOMED-WS

(tylosin tartrate)

Soluble Powder

Chickens, Turkeys, Swine, and Honey Bees

The effect of the supplement is to add indications to the product label for swine to include: For the treatment and control of swine dysentery associated with *Brachyspira hyodysenteriae* when followed immediately by tylosin phosphate Type A medicated article in feed, and for the control of porcine proliferative enteropathies (PPE, ileitis) associated with *Lawsonia intracellularis* when followed immediately by tylosin phosphate Type A medicated article in feed.

Sponsored by:

Cross Vetpharm Group Ltd.

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I. GENERAL INFORMATION:

A. File Number: ANADA 200-455

B. Sponsor:

Cross Vetpharm Group Ltd.
Broom Hill Rd.
Tallaght, Dublin 24
Ireland

Drug Labeler Code: 061623

U.S. Agent:
Ms. Linda Duple
Bimeda Inc.
2836 Dolliver Park Avenue
Lehigh, IA 50557

C. Proprietary Name: TYLOMED-WS

D. Established Name: Tylosin tartrate

E. Pharmacological Category: Antimicrobial

F. Dosage Form: Soluble powder

G. Amount of Active Ingredient: 100 grams of tylosin tartrate per pouch or jar or
256 grams of tylosin tartrate per pouch or jar

H. How Supplied: 100 gram pouch and jar
256 gram pouch and jar

I. How Dispensed: OTC

J. Dosages:

Chickens: 2 grams per gallon; should be treated for three days; however, treatment may be administered for one to five days depending on the severity of infection. Treated chickens should consume enough medicated drinking water to provide 50 milligrams (mg) tylosin per pound body weight per day. Only medicated water should be available to birds.

Turkeys: 2 grams per gallon; should be treated for three days; however, treatment may be administered for 2 to 5 days depending on the severity of infection. Treated turkeys should consume enough medicated drinking water to provide 60 mg tylosin base per pound body weight per day. Only medicated water should be available to birds.

Swine: For the treatment and control of swine dysentery medicate with 250 mg tylosin per gallon in drinking water for 3 to 10 days, depending upon severity of infection. Alternatively, medicate with 250 mg tylosin per gallon in drinking water for 3 to 10 days, followed by 40 to 100 g of tylosin per ton of complete feed (Type C medicated feed manufactured from tylosin phosphate Type A medicated article) for 2 to 6 weeks. For control of porcine proliferative enteropathies (PPE, ileitis) medicate with 250 mg tylosin per gallon in drinking water for 3 to 10 days, followed by 40 to 100 g of tylosin per ton of complete feed (Type C medicated feed manufactured from tylosin phosphate Type A medicated article) for 2 to 6 weeks. Swine must consume enough medicated water to provide a therapeutic dose. Only medicated water (250 mg tylosin per gallon) should be available while medicating with TYLOMED-WS.

Honey Bees: Mix 200 milligrams tylosin in 20 grams confectioners/powdered sugar. Use immediately. Apply (dust) this mixture over the top bars of the brood chamber once weekly for 3 weeks.

K. Route of Administration: Oral in water for chickens, turkeys, and swine. Oral in confectioners/powdered sugar for honey bees.

L. Species/Class: Chickens, turkeys, swine, and honey bees.

M. Indications:

Chickens: As an aid in the treatment of chronic respiratory disease (CRD) associated with *Mycoplasma gallisepticum* sensitive to tylosin in broiler and replacement chickens. For the control of CRD associated with *Mycoplasma gallisepticum* sensitive to tylosin at the time of vaccination or other stress in chickens. For the control of CRD associated with *Mycoplasma synoviae* sensitive to tylosin in broiler chickens.

Turkeys: For maintaining weight gain and feed efficiency in the presence of infectious sinusitis associated with *Mycoplasma gallisepticum* sensitive to tylosin.

Swine: For the treatment and control of swine dysentery associated with *Brachyspira hyodysenteriae*. For the treatment and control

of swine dysentery associated with *Brachyspira hyodysenteriae* when followed immediately by tylosin phosphate Type A medicated article in feed. For the control of porcine proliferative enteropathies (PPE, ileitis) associated with *Lawsonia intracellularis* when followed immediately by tylosin phosphate Type A medicated article in feed.

Honey Bees: For the control of American Foulbrood (*Paenibacillus larvae*).

N. Reference listed new animal drug:

TYLAN Soluble; tylosin tartrate; NADA 013-076; Elanco Animal Health, A Division of Eli Lilly & Co.

O. Effects of Supplement:

This supplement provides for addition of two swine indications on the RLNAD labeling whose marketing exclusivity expired. They are: For the treatment and control of swine dysentery associated with *Brachyspira hyodysenteriae* when followed immediately by tylosin phosphate Type A medicated article in feed, and for the control of porcine proliferative enteropathies (PPE, ileitis) associated with *Lawsonia intracellularis* when followed immediately by tylosin phosphate Type A medicated article in feed.

The "Directions for Use" has changed due to the addition of the swine indications. These changes in directions include: For the treatment and control of swine dysentery medicate with 250 mg tylosin per gallon in drinking water for 3 to 10 days, depending upon severity of infection. Alternatively, medicate with 250 mg tylosin per gallon in drinking water for 3 to 10 days, followed by 40 to 100 g of tylosin per ton of complete feed (Type C medicated feed manufactured from tylosin phosphate Type A medicated article) for 2 to 6 weeks. For control of porcine proliferative enteropathies (PPE, ileitis) medicate with 250 mg tylosin per gallon in drinking water for 3 to 10 days, followed by 40 to 100 g of tylosin per ton of complete feed (Type C medicated feed manufactured from tylosin phosphate Type A medicated article) for 2 to 6 weeks. Swine must consume enough medicated water to provide a therapeutic dose. Only medicated water (250 mg tylosin per gallon) should be available while medicating with TYLOMED-WS.

II. BIOEQUIVALENCE:

Under the provisions of the Federal Food, Drug, and Cosmetic Act, as amended by the Generic Animal Drug and Patent Term Restoration Act of 1988, an abbreviated new animal drug application (ANADA) may be submitted for a generic version of an approved new animal drug (reference listed new animal drug). New target animal safety and effectiveness data and human food safety data (other than tissue residue data) are not required for approval of an ANADA.

Ordinarily, the ANADA sponsor is required to show that the generic product is bioequivalent to the RLNAD, which has been shown to be safe and effective. If bioequivalence is demonstrated through a clinical endpoint study, then a tissue residue study to establish the withdrawal time for the generic product should also be conducted. For certain dosage forms, the agency will grant a waiver from the requirement of an *in vivo* bioequivalence study. (55 FR 24645, June 18, 1990; Fifth GADPTRA Policy Letter; Bioequivalence Guideline, October 9, 2002).

Based on the formulation characteristics of the generic product, Cross Vetpharm Group Ltd. was granted a waiver from the requirement for an *in vivo* bioequivalence study for the generic product TYLOMED-WS (tylosin tartrate) soluble powder. The generic product is administered orally in water for chickens, turkeys, and swine, and orally in confectioners/powdered sugar for honey bees, and contains the same active ingredient in the same concentration and dosage form as the RLNAD, and contains no inactive ingredients that may significantly affect the absorption of the active ingredient.

III. EFFECTIVENESS:

CVM did not require effectiveness studies for this supplemental approval.

IV. TARGET ANIMAL SAFETY

CVM did not require target animal safety studies for this supplemental approval.

V. HUMAN FOOD SAFETY:

The following are assigned to this product for chickens, turkeys, swine, and honey bees:

- **Tolerances for Residues:**
  The tolerances established for the pioneer product apply to the generic product. A tolerance of 0.2 parts per million (ppm) (negligible residue) is established for tylosin residues in eggs and the uncooked edible tissues in fat, muscle, liver, and kidney of chickens, turkeys, and swine under 21 CFR 556.740.
- **Withdrawal Times:**
  Because a waiver of the *in vivo* bioequivalence study was granted, the withdrawal times are those previously assigned to the pioneer product.

  Withdrawal periods have been established for the indicated species: 24 hours for chickens, 5 days for turkeys, 48 hours for swine, and 4 weeks before main honey flow in honey bees for tylosin tartrate (21 CFR 520.2640).

- **Regulatory Method for Residues:**
  The analytical method for the determination of tylosin residues in tissues uses a microbiological assay procedure. This method is found in the Food Additives

Analytical Manual on file at the Center for Veterinary Medicine, 7500 Standish Place, Rockville, MD 20855.

The analytical method for the determination of tylosin in honey is a microbiological assay using an oxytetracycline-resistant strain of *Paenibacillus larvae* in tissues (the causative agent of American foulbrood disease of honey bees). A copy of the method is on file at Center for Veterinary Medicine, 7500 Standish Place, Rockville, MD 20855.

VI. USER SAFETY:

CVM did not require user safety studies for this supplemental approval.

The product labeling contains the following information regarding safety to human handling, administering, or exposed to TYLOMED-WS:

"Not for use in humans. Keep out of reach of children."

VII. AGENCY CONCLUSIONS:

This information submitted in support of this ANADA satisfies the requirements of section 512(n) of the Federal Food, Drug, and Cosmetic Act and demonstrates that TYLOMED-WS, when used according to the label, is safe and effective.